

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	EU-funded initiatives for Real World Evidence: descriptive analysis of their characteristics and relevance for regulatory decision making
<b>AUTHORS</b>	Plueschke, Kelly; McGettigan, Patricia; Pacurariu, Alexandra; Kurz, Xavier; Cave, Alison

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Marc Berger Independent Consultant USA
<b>REVIEW RETURNED</b>	15-Feb-2018

<b>GENERAL COMMENTS</b>	This is a nice summary of the state of affairs with respect to EU-funded initiatives linked to 'Real World Evidence' (RWE) that looks at the potential for their outputs to support regulatory decision making on medicines. As such it provides a useful summary. However, the authors should be more detailed and expansive regarding the impact (or lack thereof) of these initiatives and how they could be improved going forward. If a survey were done of end-users of these initiatives, I think the majority would believe that they really didn't deliver much in terms of impact; and that the majority were not sustainable. Why is that? Moreover, if the overarching goal is to develop an infrastructure of real world data collection to support the development of real world evidence to inform regulatory decision making, then exactly what would be required? Would the list of initiatives -- even if they all were wildly successful -- meet this goal? Is the problem a matter of execution or ambition or both?
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<b>REVIEWER</b>	Shirley Wang Brigham and Women's Hospital, Harvard Medical School
<b>REVIEW RETURNED</b>	20-Feb-2018

<b>GENERAL COMMENTS</b>	In figure 1 there are two asterisks next to "selection" in step 1 with the dates Sept 2016-Dec 2016. This seems like it refers to dates during which the search and review was conducted, but there is no corresponding footnote for the asterisks. It would also be relevant to be clear about the span of time that was included in the search. In the manuscript text, does "the search cut-off date" of Dec 31st 2016 mean that everything for all time before end of 2016 was searched?
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<b>REVIEWER</b>	Alex Sverdlov Novartis, USA
<b>REVIEW RETURNED</b>	01-Mar-2018

<b>GENERAL COMMENTS</b>	The paper is very well written. My only suggestion for the authors is
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	to consider adding a sentence on how the results of the current study can be useful to other stakeholders such as sponsors, patients, and advocacy groups.
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### VERSION 1 – AUTHOR RESPONSE

Answer to Reviewer 1: We agree with the comments. We have modified the following line in order to emphasise the current lack of impact of these initiatives on regulatory procedures, as well as proposed some suggestions on how to better exploit them.

Revised lines: 233-238, 268 – 271, 275-279, 286-293, 300-303, 363-365

Answer to Reviewer 2: We agree with the comments. We have updated Figure 1 (referred to in line 146) accordingly by removing the 2 asterisks. The span time has also been clarified throughout the document. The search cut-off date was 31st December 2016, meaning that all initiatives matching the keywords that began before or on that date (and that were funded by either the EU or national bodies) were included.

Revised lines: 48, 112-114, 191, 221-222, 371

Answer to Reviewer 3: We agree with the comment and have revised lines 275-277 to clarify the stakeholders who might like to consider the options put forward in our manuscript to better exploit the outcomes of publically funded initiatives.

In addition, the following lines have been updated:

- Words count: line 15
- Typos or missing words corrected on lines 149, 175, 224, 294-295, 315
- Footnotes on lines: 379, 381, 384, 399-400, 401

### VERSION 2 – REVIEW

<b>REVIEWER</b>	Marc Berger Private Consultant
<b>REVIEW RETURNED</b>	30-Mar-2018

<b>GENERAL COMMENTS</b>	The authors have nicely addressed reviewer comments.
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<b>REVIEWER</b>	Shirley Wang Brigham and Women's Hospital, Harvard Medical School
<b>REVIEW RETURNED</b>	09-Apr-2018

<b>GENERAL COMMENTS</b>	Thank you for addressing minor comments. This is an important contribution scientific literature.
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